REMARKS/ARGUMENTS

In the specification, the paragraph beginning on page 13, line 31 and ending on page 14, line 7 has been amended to delete the embedded hyperlinks and/or other forms of browser-executable code pusuant to MPEP § 608.01.

In amended Figure 12, sequence identifiers, SEQ ID NOs.: 7 and 8, have been added.

Support for the amendments to claims 1 and 2 can be found throughout the specification, for example, on page 12, lines 8-12, lines 18-20, and lines 23-25. Claims 9-12 were amended to correct a typographical error.

Claims 1-48 are pending in this application. Claims 6-8 and 13-48 are withdrawn, as being drawn to nonelected inventions. Claims 1-5 and 9-12 are rejected.

REJECTION OF THE CLAIMS UNDER 35 U.S.C. §101

Claims 1-5 and 9-12 are rejected under 35 U.S.C. §101, as being directed to non-statutory subject matter. According to the Examiner, the claimed method is non-statutory subject matter, because it "is neither a method of making or a method of using". Further, the Examiner contends that it is not clear what the "utility is of the method of simply expressing a plurality of proteins" The Examiner acknowledges that claims 3-5 fulfill the utility requirement.

In reply, Applicants respectfully submit that claims 1 and 2 have been amended to recite a method of producing a protein having an activity or property of interest. Therefore, Applicants respectfully submit that claims 1, 2, 9-12 as amended meet the utility requirement, as do claims 3-5.

In view of these amendments, Applicants respectfully request that the Examiner withdraw the rejection under 35 U.S.C.§101.

REJECTION OF THE CLAIMS UNDER 35 U.S.C.§112, SECOND PARAGRAPH

Claims 1-5 and 9-12 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to distinctly claim the subject matter which applicant regards as the invention. The Examiner contends that in claim 1 the process step of "providing" is unclear, because it is not a "positive, manipulative process step". According to the Examiner, "it is unclear whether it relates to a step of making the

fungal in suspension or its transferable reproductive elements or an already prepared (i.e. supplied by applicants) fungi, especially in connection with step (e)." Also, the Examiner contends that "Plurality of individual fungal" and "at least one heterologous protein encoding nucleic acid" lack antecedent basis.

In reply, Applicants respectfully submit that claim 1 has been amended to more clearly claim the subject matter of the invention. Applicants have deleted the phrase "provide a filamentous fungus" in claim 1 and replaced it with "prepare a filamentous fungal suspension...". Applicants have also added the appropriate antecedent basis for the phrase "plurality of individual fungal", and have deleted the word "heterologous" so that the amended phrase "at least one protein encoding nucleic acid" has the appropriate antecedent basis.

In view of these amendments, Applicants respectfully request that the Examiner withdraw the rejection under 35 U.S.C. § 112, second paragraph.

REJECTION OF THE CLAIMS UNDER 35 U.S.C.§102(e)

Claims 1-5 are rejected under 35 U.S.C. § 102(e), as being anticipated by Borchert et al. US Patent No. 6,518,042. The Examiner contends that

> Borchert discloses at col. 2, line 55 to col. 3, line 41; col. 8, lines 36-30, a method for producing a polypeptide of interest comprising the steps of a) preparing a filamentous fungal cell population wherein individual cells in the population comprise individually different DNA sequences of interest representing a DNA library of interest comprising placing individually different DNA sequences of interest in a filamentous fungal cell population; b) growing the population of the fungal cells for a period of time allowing an individual DNA sequence of interest in the population to be duplicated and wherein the DNA sequences of interest encode a polypeptide of interest, and c) selecting from the resultant population of filamentous fungal cells the desired polypeptide of interest. See the specific Examples at col. 11, lines 20 up to col. 16, line 63. See specifically the spore-suspension of the fungal cells being made which will read on the broad claimed transferable reproductive elements. Accordingly, the specific process steps of Borchert using specific components of e.g., fungal cells and nucleic acids fully meet the broad claimed method.

With all due respect, Applicants disagree. The Borchert et al. patent describes a process for making DNA libraries in a conventional filamentous fungal host cell preparation where the fungal host cell has an inactivated mismatch repair system gene. There is *nothing* in Borchert which teaches or suggests the use of low-viscosity fungal cells that are characterized by growth in suspension and the ability to produce transferable reproductive elements in suspension. Applicants have amended claim 1 to include the phrase "low-viscosity" to further define this feature of the invention. In Borchert, once the fungi have been transformed, and the transformants selected for, it is necessary to prepare spores or to otherwise mechanically disrupt the fungal cells, in order to disperse the library of transformed fungi into individual organisms or reproductive elements. Such procedures are labor intensive and not amenable to automation. Applicants' invention entirely avoids the step of preparing a spore suspension. The phenotype of Applicants' claimed fungal cells allows culturing of filamentous fungi under conditions conducive to the formation of transferable reproductive elements in suspension, dispensing with the need for mechanically or chemically disrupting the culture to obtain individual reproductive elements. Therefore, Borchert does not anticipate Applicants' claimed invention. Further, as a result of Applicants' invention, efficient screening of fungally-expressed proteins can now be accomplished. Borchert neither teaches or suggests these aspects of the claimed invention.

In view of the amendment and remarks presented above, Applicants respectfully request that the Examiner withdraw the rejection under 35 U.S.C. § 102(e).

REJECTION OF THE CLAIMS UNDER 35 U.S.C.§103

Claims 1-5 and 9-12 are rejected under 35 U.S.C.§103(a) as being unpatentable over Borchert et al. U.S. Patent No. 6,518,042 or Applicants' disclosure of known prior art (as applied to the elected species, hyphal fragments). The Examiner contends

> Borchert et al or the prior art disclosed by applicants does not teach hyphal fragments (some of the prior art disclosed by applicants described this fragment.). However, Shuster discloses at col. 4, line 38

> up to col. 5, line 5 said mutant cells having a more extensive hyphal branching. Shuster further discloses that the mutant cells have an improved property for production of a heterologous polypeptide than the parent cell, when the mutant and the parent cells are cultured under the same conditions. The mutants possess improved growth characteristics in fermentation where the morphology gives rise to lower viscosity in the fermenter, in turn leading to easier mixing, better aeration, better growth, and ultimately, enhanced yield of heterologous polypeptide produced by the mutant strain relative to the parent strain. In a preferred embodiment, the improved property is selected from the group consisting of (a) increased yield of the heterologous polypeptide, (b) improved growth, (c) lower viscosity, and (d) better secretion. In a most preferred embodiment, the improved property is increased yield of the heterologous polypeptide. In another most preferred embodiment, the improved property is improved growth. In another most preferred embodiment, the improved property is lower viscosity. In another most preferred embodiment, the improved property is better secretion. Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use a hyphal fragment in the method of Borchert or anyone of the prior art disclosed by applicants in the manner as taught by Schuster et al. One would have been motivated to use a hyphal fragment rather than the whole cell for the lower viscosity and better secretion of the heterologous DNA as taught by Shuster.

As stated above, nothing in Borchert et al. teaches or suggests the use of low-viscosity fungal cell cultures that are capable of producing transferable reproductive elements in suspension. Moreover, Shuster does not cure the deficient teaching of Borchert et al. Shuster teaches methods of obtaining mutant cells from a conventional filamentous fungal parent cell, and identifying the mutant cells which exhibit more extensive hyphal branching, which in turn leads to mutants that have improved properties for the production proteins. Shuster does not teach or suggest the formation of transferable reproductive elements (e.g. hyphal fragments). Furthermore, Shuster does not teach or suggest the use of low-viscosity cultures to facilitate separation of the individual reproductive elements, or the subsequent

culturing of those individual elements into monoclonal cultures for use in efficient screening methods.

An important aspect of the present invention involves the use of both low-viscosity fungal cultures and the formation of transferable reproductive elements. Neither element by itself is sufficient to obtain cultures that can be efficiently screened. Accordingly, the Shuster patent, which only addresses low-viscosity cultures and their advantages for improved protein production and secretion, does not teach or suggest the present invention.

Applicants' respectfully disagree with the Examiner's conclusion that it would have been obvious to one of ordinary skill in the art to use a hyphal fragment in the method of Borchert as taught by Shuster, because, as stated above, Shuster does not teach hyphal fragments. For the same reasons, there would have been no motivation to combine the teachings of Borchert and Shuster because the two references comprise non-overlapping subject matter, with no suggestion on the part of either to utilize the respective teachings to facilitate high-throughput screening.

In view of the remarks presented above, Applicants' respectfully request that the Examiner withdraw the rejection under 35 U.S.C.§103(a)

Applicants believe that the claims are currently in condition for allowance. Examination on the merits and passage to issue is respectfully requested.

Respectfully submitted,
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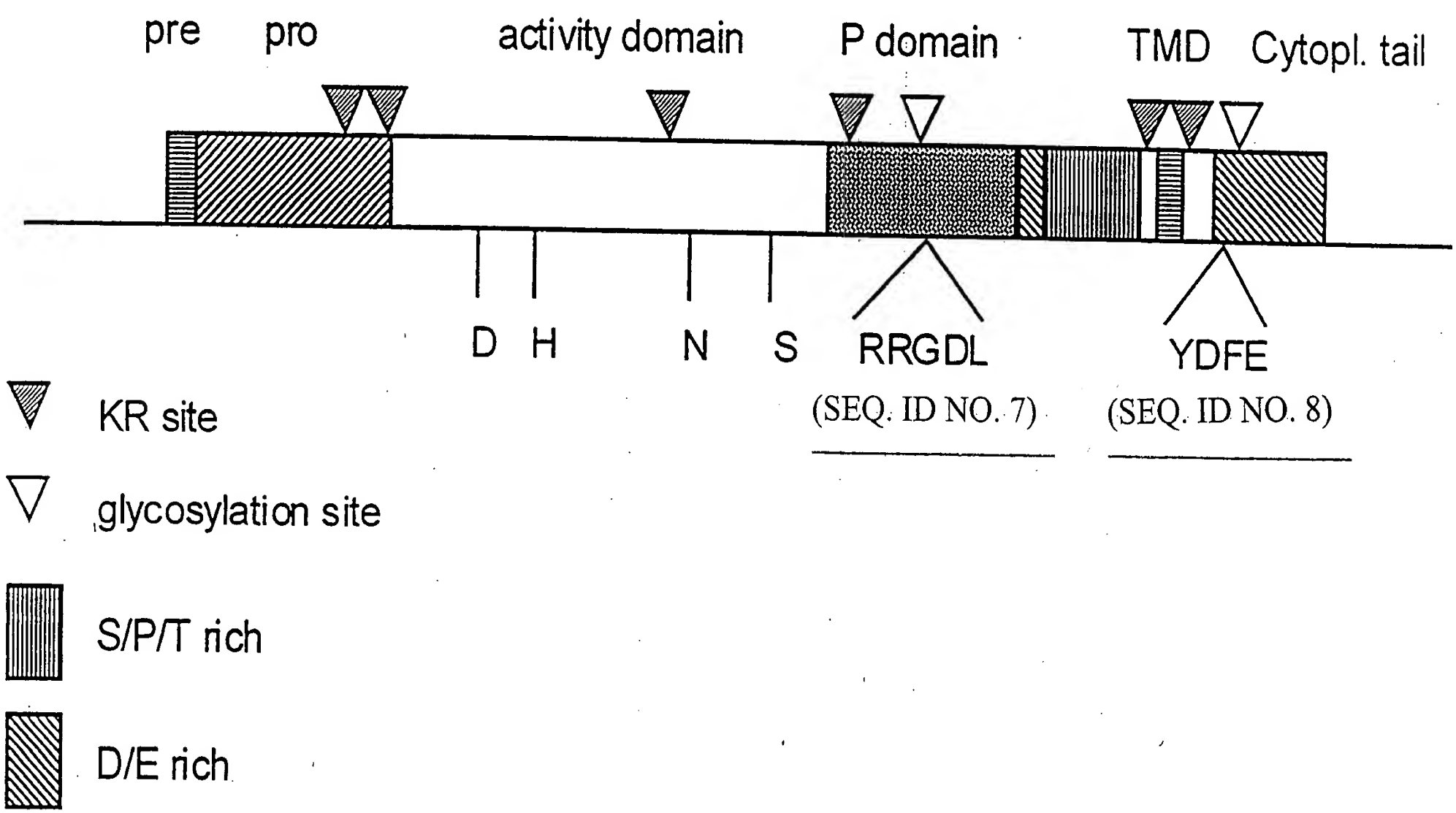

Fig 12